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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/691,237	10/19/2000	David S. Wells	085747/0170	5026

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1615	21

DATE MAILED: 12/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/691,237	Applicant(s) WELLS ET AL.	
	Examiner Lakshmi S Channavajjala	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *35-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Receipt of request for extension of time; request under 37 CFR 1.114 and preliminary amendment C, dated 9-9-03 is acknowledged.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9-9-03 has been entered.

Claims 1-34 have been canceled. New claims 35-59 have been presented.

Claim Rejections - 35 USC § 112

Claims 35-59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Instant claims present the limitation, "a single layer core matrix of a therapeutically active agent and a gelling agent, wherein the amount of active agent and gelling agent together is about 30-90% w/w of the composition", which is a new matter. Applicants pointed out in their remarks section that the limitations find literal support on page 14, lines 4-15. However, a careful

examination of the above page does not show support for single layer core matrix. Instant specification does not state that the matrix is a single layer or that it should not contain more than a single layer. Applicants state that the support is inherent. However, the specification is silent of any number of layers of matrix thus allowing for either a single layer or multiple layers to be present. Therefore, the limitation is considered a new matter.

Claim Rejections - 35 USC § 103

Claims 35-38, 40-48, 50-53 and 55-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,366,738 to Rork et al (Rork) in view of US 6,589,994 to Balandrin et al (Balandrin).

Rork teaches a controlled release formulation that provides delivery of drugs independent of their solubilities. The formulation of Rork comprises of a core containing drug and a water swellable polymer; and a coating of water insoluble polymer surrounding the core (col. 4, lines 4-34). The formulations delivers drug over four to twenty hour period (see figures). Rork suggests both water-soluble as well as insoluble drugs (col. 5, lines 32-32) including hypnotics and sedatives such as diethylisovaleramide or bromo-isovaleryl-urea (col. 6, lines 15-19). The admixture of drug and polymer reads on the matrix of the instant claims. Rork teaches that the coating around the core is impermeable and insoluble and forms films (col. 4) and the coating includes plasticizers (claims). Further, Rork teaches polymer coating be made of polymers such as ethyl cellulose, cellulose acetate etc (claim 9, lines 48-62). Rork teaches diethylisovaleramide and not isovaleramide or isovaleric acid, as claimed. Further, Rork teaches the amounts of

polymer and drug in a range that includes the claimed range (col. 7, lines 34 through col. 8, lines 21) and also teaches the preparation of the dosage form by compression (col. 8-9).

Balandrin teaches isovaleramide, isovaleric acid and other structurally related compounds that exhibit clinically significant pharmacological activity, in treating disorders such as convulsions, spasticity and others ameliorated by CNS activity (col. 2, lines 7-47). Balandrin teaches various amounts of isovaleramide or its related compounds and suggests optimizing the amount administered depending on the severity of the conditions (for example, number and duration of convulsions) (col. 15). Balandrin teaches oral administration of isovaleramide in the form of tablets, capsules or drops etc (col. 15). Balandrin does not teach instant sustained release dosage form.

It would have been obvious for a skilled artisan at the time of the instant invention to use isovaleramide or isovaleric acid or other structurally related compounds exhibiting the same pharmacological activity, of Balandrin in place of or together with diethylisovaleramide in the sustained release composition of Rork because Balandrin suggests all the other compounds are equally effective in rendering therapy for CNS mediated disorders. Alternatively, Balandrin teaches isovaleramide for a number of other CNS disorders, but does not teach controlled release compositions. However, it would have been obvious for a skilled artisan at the time of the instant invention to use the controlled release polymer and film coating s of Rork in preparing a formulation of isovaleramide of Balandrin, with an expectation to provide the drug delivery over a period of 4 to 20 hours at a desired rate because Rork suggests that irrespective of the solubility of active agent, the swellable polymer in the core enables the release of the active agent at a relatively constant and predetermined pattern and that predictably varying amounts of the agent

can be dispensed over a specified time. One of an ordinary skill in the art would have expected to provide a constant release of diethylisovaleramide, such that the sedation or hypnotic effect of diethyisovaleramide is achieved for a long period of time.

2. Claims 39, 49 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rork et al and Balandrin et al as applied to claims 35-38, 40-48, 50-53 and 55-59 above, and further in view of Pankhania et al (5,415,871).

Neither Balandrin nor Rork teach xanthan gum as a gelling agent.

Pankhania teaches xanthan gum as a gelling agent in sustained formulations for various pharmaceutically active agents such as sedatives, cardiovascular agents etc (col. 4, lines 25-45). Pankhania suggests that xanthan gum hydrates and swells upon exposure to water, to form a gel, and allows a slow and sustained release of the active agent into the body, for as long as 24 hours or longer (col. 2 and col. 4). Pankhania also teaches that xanthan gum avoids the problems of hydrating too rapidly or too slowly and thus does not exhibit the problems of breaking up of the tablet (col. 2). Therefore, it would have been obvious for a skilled artisan at the time of the instant invention to use xanthan gum a gel forming polymer in the sustained release composition of Rork, containing diethylisovaleramide (Rork) or isovaleramide (Balandrin), because Pankhania suggests that xanthan gum as a gelling agent exhibits optimum hydration properties and the sustained release of the drug from xanthan gum containing formulation has a release profile which is independent of temperature, pH and also allows a steady diffusion of the drug.

Response to Arguments

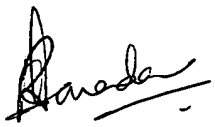
Applicant's arguments filed 9-9-03 have been fully considered but they are not persuasive.

Applicants argue that Rork teaches a two-layered matrix core and Balandrin does not specify any formulation at all. Applicants also argue that the claimed high load of drug (for a water soluble drug) is not taught by the cited art. However, applicants' attention is directed to different patents to Rork as well as Balandrin (which are different from previous rejection) used in the instant rejection. Rork clearly teaches that the controlled release dosage form works with all drugs irrespective of their solubility. Besides, Rork also states that drug amount upto 50% can be used in the dosage form. Further, instant Rork teaches a core containing drug and polymer surrounded by a film-coating, suggesting that drug and polymer constitute one layer. Applicants argue that Pankhania does not teach or suggest the claimed formulation having 30-90% active compound and gelling agent. However, Rork suggests using core polymer in claimed amounts and the advantage of adding the xanthan gum of Pankhania in the composition of Rork comes from the teaching of Pankhania that xanthan gum does not hydrate too fast or too slow, exhibiting optimum hydration and thus avoid the breaking up of tablets.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S Channavajjala whose telephone number is 703-308-2438. The examiner can normally be reached on 7.30 AM -4.00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-7924 for regular communications and 703-308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.



Lakshmi S Channavajjala
Examiner
Art Unit 1615
November 24, 2003